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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/822,161	03/30/2001	Michael Detmar	MGH 1512 CIP	6294
21874	7590	02/25/2005	EXAMINER	
EDWARDS & ANGELL, LLP P.O. BOX 55874 BOSTON, MA 02205			HARRIS, ALANA M	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 02/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/822,161

Applicant(s)

DETMAR ET AL.

Examiner

Alana M. Harris, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 May 2004 and 24 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 22 and 23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 22 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>duplicates, 3/29/04 and 05/13/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 13, 2004 has been entered.

2. Claims 1-5, 7, 22 and 23 are pending.

Claims 6, 16-22 and 24-29 have been cancelled.

Claims 1, 2, 5, 7, 22 and 23 have been amended.

Claims 1-5, 7, 22 and 23 are examined on the merits.

Withdrawn Rejections and Objections

Claim Objections

3. Claim 26 is no longer objected to under 37 CFR 1.75 as being a substantial duplicate of claim 6 because both claims have been cancelled.

Claim Rejections - 35 USC § 112

4. The rejection of claims 27-29 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

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reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn because the claims have been cancelled.

5. The rejection of claims 1-5, 7 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for treatment of tumor using cell matrix structure comprises a matrix having attached thereto cells expressing TSP-2, does not reasonably provide enablement for any other anti-angiogenic molecule for tumor or any other diseases is withdrawn in light of Applicants' amendments to the claims. Claims 6, 16-22 and 24-29 have been cancelled.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-5, 7, 22 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent number 6,558,422 B1 (effective filing date March 26, 1999), and further in view of U.S. Patent number 5,759,830 (issued June 2, 1998/ IDS reference BA, submitted August 22, 2002) and Gilbert et al. (Transplantation, 56(2): 423-427, August 1993/ IDS reference AD, submitted August 22, 2002). U.S. Patent

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number 6,558,422 B1 teaches examples of structures and medical devices that are completely or partially implantable into a living body, see abstract. The medical device contains biologically active substance(s) such as thrombospondins and functional domains of the said proteins within the indentation surface layer of a matrix structure, see bridging paragraph of columns 2 and 3; column 4, lines 1-22. The implantable medical devices include polymers, scaffolds that support tissue growth and indentations formed by micromechanical machining, see bridging paragraph of columns 4 and 5; column 5, lines 18-31; bridging paragraph of columns 6 and 7; column 7, lines 16-51; bridging paragraph of columns 8 and 9. Particularly, rats were treated with implantable devices, disks containing thrombospondin-2 (TSP-2) wherein angiogenesis and fibrous capsule measurements were reduced, see column 11, lines 5-22; column 12, line 52-column 13, line 14; and Table 5 in column 13. The '422 patent does not teach the implantation of a cell-matrix structure wherein the cells are fibroblasts, tissue specific cells or of a different cell type than the tissue that has proliferated and the cells are genetically altered to produce TSP-2 or a fragment thereof.

However, U.S. Patent #5,759,830 does teach the implementation of cells including tissue specific and fibroblastic cells for the assembly of fibrous cell scaffolds useful in implantation, see column 4, lines 15-20; column 6, lines 21-34; bridging paragraph of columns 11 and 12. The cells can be manipulated by those skilled in the art of genetic engineering in order to introduce new genes to make absent protein products, see column 9, lines 20-32.

Moreover, Gilbert teaches the cell transplantation of genetically altered cells on

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fibrous biodegradable polymer scaffolds, see title and abstract. The system is capable of delivering desirable proteins secreted by genetically modified fibroblast cells. "The polymer scaffold allows precise surgical manipulation and site-specific transplantation with subsequent incorporation of the transduced cells into the native tissue over time.", see bridging paragraph of pages 423 and 424.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of both patents and Gilbert in order to treat a disorder characterized by excessive proliferation of tissue with an implantable cell-matrix structure having attached thereto cells that stably express TSP-2 or a fragment thereof able to inhibit or regress excessive tissue proliferation. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in both patents and Gilbert based on the successful treatment of rats in which angiogenesis and fibrous growth were reduced, as well as the implicit teaching that biologically active substances can be used to form layers within indentation surfaces and on implantable medical devices placed within a living body, see patent '422, column 4, lines 1-25; column 5, lines 11-19. It is within the Examiner's purview that substances that form layers are inclusive of cells. Moreover, patent '830 presents information stating the taught method is useful both *in vivo* and *in vitro* and medical conditions can be corrected by insertion of genes, see column 22, lines 16-27; column 9, lines 20-32. Likewise, Gilbert suggests "[t]he application of cell transplantation and retroviral gene transfer technologies may lead to the eventual cure of many gene product deficiencies resulting from a single gene defect...", page 425,

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column 2, first paragraph of the Discussion section. Clearly one of ordinary skill in the art would have been motivated to combine the teachings of all the references for the successful treatment of any disorder characterized by excessive proliferation of tissue based upon the accomplished treatment in patent '422 and the level of knowledge in the area of genetic engineering at the time of the claimed invention was made presented in patent '830 and Gilbert.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner works a flexible schedule, however she can normally be reached between the hours of 6:30 am to 5:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER


Alana M. Harris, Ph.D.
20 February 2005